510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE

A. 510(k) Number:
k033458

B. Analyte:
Confirmatory ESBL Test -AST

C. Type of Test:
Antimicrobial Susceptibility Test (AST) colorimetric oxidation-reduction, growth-based, qualitative results.

D. Applicant:
Becton, Dickinson and Company

E. Proprietary and Established Names:
BD Phoenix™ Automated Microbiology System

F. Regulatory Information:

1. Regulation section:
   CFR 866.1645 Short Term Antimicrobial Susceptibility Test System
2. Classification:
   Class II
3. Product Code:
   LON Automated short incubation AST system
4. Panel:
   83 Microbiology

G. Intended Use:

1. Intended use(s):
   The BD Phoenix™ Automated Microbiology System is intended for *in vitro* quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC)of most Gram-negative aerobic and facultative anaerobic bacteria isolates from pure culture for *Enterobacteriaceae* and Non-*Enterobacteriaceae* and most Gram-positive bacteria isolates from pure culture belonging to the genera *Staphylococcus* and *Enterococcus*.

   The BD Phoenix™ GN Panel: The BD Phoenix™ Automated Microbiology System is intended for the *in vitro* rapid identification (ID) and quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of gram negative aerobic and facultative anaerobic bacteria belonging to the family *Enterobacteriaceae* and non-*Enterobacteriaceae*.

2. Indication(s) for use:
   This submission is for the addition of the confirmatory ESBL Test to Gram-negative ID/AST or AST BD Phoenix™ panels. The Phoenix™ Confirmatory ESBL Test is a confirmatory test for the detection of the organisms that produce extended spectrum β-lactamase (ESBL) in *Escherichia coli, Klebsiella pneumoniae* and *Klebsiella oxytoca*.
3. Special condition for use statement(s):
   For prescription use.
4. Special instrument Requirements:
   Not applicable

H. Device Description:

The BD Phoenix™ System includes instrumentation and software, sealed and self-inoculating molded polystyrene trays with 136 micro-wells containing dried reagents, and specific inoculum broth formulations for ID and AST Indicator. The organism to be tested must be a pure culture and be preliminarily identified as gram positive or gram negative. Colonies are then suspended in broth, and equated to a 0.5 McFarland with the recommendation to use the BD CrystalSpec™ Nephelometer. A further dilution is made into an AST broth, which contains an AST indicator, prior to inoculating the panel. The AST broth is a cation-adjusted formulation of Mueller-Hinton broth containing 0.01% Tween 80. After adding the indicator solution to the AST inoculum the color is blue and after inoculation and incubation goes to pink to colorless as reduction in the panel well proceeds. Inoculated panels are barcode scanned and loaded into the BD Phoenix™ Automated Microbiology System instrument where the panels are continuously incubated at 35^{o}C. The AST has a final inoculum of 5×10^{5} CFU/ml. The instrument incubates, reads and records the results of the biochemical substrates and antimicrobial agents and interprets the reactions to give an ID of the isolate and category interpretation for the presence or absence of ESBL The ESBL test uses the principle of clavulanate inhibition of ESBLs in combination with cephems. The test compares the maximum growth rate observed in the test wells in relation to the growth control well on the panel to determine growth or inhibition with a certain antimicrobial agent. The classification tree algorithm compares these relative growth rates to a series of thresholds in the decision tree. Additional interpretation is done using a software driven "EXPERT " System using rules derived from the NCCLS documentation.

Readings are taken every 20 minutes with an ID result available between 2-12 hours and an AST result available between 4-16 hours. This is only an autoread result; there are no manual readings possible

I. Substantial Equivalence Information:

1. Predicate device name(s):
   Sensititre ESBL confirmatory test
2. Predicate K number(s):
   k031545
3. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
Specimen	Isolated colonies from culture used	Isolated colonies from culture used
Inoculum	Inoculum density to 0.5 McFarland standard	Inoculum density to 0.5 McFarland standard
Results	Detection of ESBL by the response of the organism to clavulanate in combination with cephems for a positive or negative result	same
Panels	Dried antibiotics	Dried antibiotics
Differences		
Item	**Device**	**Predicate**
Instrumentation	Automated using Phoenix™ System	Manual or automated using Sensititre® reader.
Technology	Automated growth based enhanced by use of a redox indicator (colorimetric oxidation-reduction) to detect organism growth with use of a tree algorithm that includes some screen antibiotics and clavulanate with out the use of actual MIC reduction comparisons to determine the presence of ESBL.	Growth based with and without clavulanic acid using MIC values to determine reduction of growth.
Incubation	<16 hours	$\geq$ 16 hours
Antibiotics as part of the determination	Set concentrations of Ceftriaxone Cefotaxime Ceftazidime plus screening antibiotics used in a decision tree	Ceftazidime/clavulanic acid at 0.06/4-128/4 ug/ml and Cefotaxime/clavulanic acid at 0.06/4-64/4 ug/ml

J. Standard/Guidance Document Referenced (if applicable):

"Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA" , NCCLS M7 (M100-S13) "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard."

K. Test Principle:

The system employs conventional, colorimetric, fluorogenic and chromogenic substrates to identify the genus and species of the isolate. The Phoenix™ ESBL test

is based on the principle of a differential response between the inhibitory effect of selected second or third generation cephalosporins in the presence or absence of β – lactamase inhibitor, clavulanic acid. When the test result of ESBL is positive, the categorical interpretation of all beta-lactam drugs, except carbapenems, on the same Phoenix™ Panel will be changed to resistant for all *E. coli, K.* pneumoniae and *K. oxytoca.*

L. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:
Inter-site and intra-site reproducibility was determined using 8 isolates tested 3 times at each of the three sites on three separate days. There were 4 ESBL producers and 4 non-ESBL producers with a reproducibility of 99.5%.

b. Linearity/assay reportable range:
Not applicable

c. Traceability (controls, calibrators, or method):
NCCLS recommended Quality Control strains were tested over 200 times each with expected results 98% of the time. The Phoenix™ results demonstrate that the system can produce the expected QC results.

Organism		Reference results	Phoenix™ results
E. coli ATCC 25922 Expected result = negative for ESBL	Neg	385	382
	Pos	3	1
K. pneumoniae ATCC 700603 Expected result = positive for ESBL			
	Neg	7	4
	Pos	388	384

Inoculum density control: The organism suspension density of the ID broth was equivalent to a 0.5 McFarland standard using the BBL™ CrystalSpec™ Nephelometer which was verified each day of testing. Internal data was used to demonstrate that the use of the BBL™ CrystalSpec™ Nephelometer would produce reproducible results. No growth rate was <1%.

d. Detection limit:
Not applicable

e. Analytical specificity:
Not applicable

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A total of 918 clinical isolates of *Klebsiella pneumoniae, Klebsiella oxytoca,* and *Escherichia coli* were recovered and tested at six sites on the Phoenix™ System and the reference method as described in the NCCLS for the detection of ESBL. The challenge data included 53 strains tested at one site and an additional 30 strains tested at a second site that were molecularly characterized.

All isolates

	Reference ESBL positive	Reference ESBL negative
Phoenix™ positive	183	32
Phoenix™ negative	6	780
	189	812
% agreement	96.8%	96.1%

The FDA guidance document, "Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA" does not really have recommendations for this test but some of the study designs were followed. (Challenge isolates, Quality Control studies and reproducibility testing). A clinical trial protocol is included. Quality Control organisms with known results were used to assess the performance of the device. Reference Broth dilution tests were prepared according to the NCCLS recommendations for ESBL confirmation are used as the reference panel for comparison.

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a and b are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The treatment confirmed positive isolates of extended spectrum β-lactamase (ESBL) in *Escherichia coli, Klebsiella pneumoniae* and *Klebsiella oxytoca* and Quality Control organisms are the same as recommended in NCCLS.

M. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.